investigators that the condition is a true degenerative one, and that it occurs so early in life because of an imperfect development of the nervous system. In other words, he accepts Gowers' term of "abiotrophy" or essential failure of vitality, and thinks that this is present as an inherited condition in these unfortunate cases. This seems to be the best explanation offered, at present, to account for the facts. Why certain children of a family are affected while others remain healthy, and why the children of Jewish parentage are especially liable to the disease, are questions which still remain to be settled.

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A PATHOLOGICAL STUDY OF AMAUROTIC FAMILY IDIOCY.[1]

By William G. Spiller, M.D.,

PROFESSOR OF NEUROPATHOLOGY AND ASSOCIATE PROFESSOR OF NEUROLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

(From the William Pepper Laboratory of Clinical Medicine, Phoebe A. Hearst Foundation, and from the Neuropathological Laboratory of the University of Pennsylvania.)

Amaurotic family idiocy is a disease that has been studied especially by American physicians. Falkenheim[2] after a careful examination of the literature has found 64 cases reported (1901), of these 47 were seen by physicians, 30 cases (24+6) occurred in America, 11 (9+2) in England, and 23 (14+9) on the Continent of Europe.

More recently (1904) Heveroch[3] has collected the records of 86 cases, of which 44 occurred in America.

B. Sachs was the first to recognize the clinical symptoms of amaurotic family idiocy, and gave the disease the name by which it is now known. It was subsequently shown that one symptom of the condition had been previously recognized by Warren Tay, who described a case presenting "symmetrical changes in the region of the yellow spot in each eye of an infant."

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[1] Read in abstract at the meeting of the American Association of Pathologists and Bacteriologists, April, 1904.

[2] Jahrbuch f. Kinderheilkunde, 1901, p. 123.

[3] Abstract in Neurologisches Centralblatt, October 16, 1904, p. 948.

In his earlier publication on this subject in 1887, Sachs supposed the disease to be due to peculiar changes in the cortical cells. Hirsch was the first to show that not only the cortical cells, but all the cells of the gray matter of the entire central nervous system were similarly affected.

I have had the opportunity to make a pathological study in a typical case of the disease that had been under the care of Dr. J. H. McKee, and had also been examined by me and others. I am much indebted to Dr. McKee for the pathological material. His necropsy notes are as follows:

"A piece of nerve was cut from the internal plantar; a piece of muscle from the flexor brevis digitorum.

"Thymus was small.

"Thyroid was well developed and presented a large isthmus.

"Pericardium: There was slight increase in the amount of the fluid.

"Heart: Both post-mortem and chicken-fat clots were found, but there were no valvular or endocardial lesions.

"Lungs: The left lung showed a massive catarrhal pneumonia of the lower lobe, and of the extreme posterior portion of the upper. The apex and free anterior border exhibited considerable emphysema. The basal portion of the lower lobe sunk in water. The right lung showed similar pneumonic changes in the lower and middle lobes.

"Pleuræ were free from adhesions or recent exudate.

"Peritoneum: Nothing abnormal was noticed, and there was no undue dryness.

"Appendix was very long and thin.

"Intestine: The small bowel exhibited intussusception (agonal?) at five places. The large bowel was small and collapsed.

"Spleen was slightly enlarged but not unduly dark. It presented no notch.

"Liver also was slightly enlarged, but remarkable in the fact that it presented none of the naked eye appearances of fatty infiltration.

"Kidneys: Nothing of interest was noticed macroscopically. Suprarenals were apparently normal.

"Lymph nodes: The peribronchial glands were enlarged and red, but the process was obviously an acute one. No caseous lymph nodes were noticed either in the thorax or abdomen.

"Brain: The subarachnoid fluid was much increased in amount. The meningeal vessels were intensely injected. The brain itself was very moist and heavy."

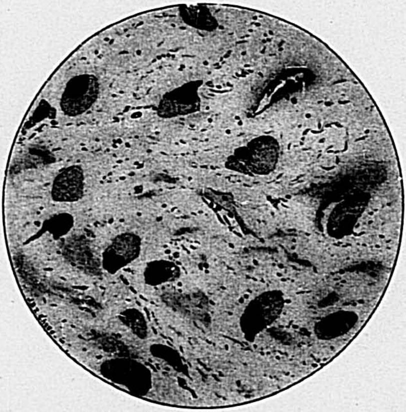
The results of my microscopic study are as follows:

The nerve cells throughout the spinal cord are much enlarged, the chromophilic elements have disappeared except about the nucleus, and here they have become granular, and in many cells the nucleus has been displaced to the periphery of the cell body. The dendritic processes of the nerve cells have disappeared in most of the cells.

The cells of the hypoglossus nucleus, of the nucleus ambiguus, of the lower olive, of the abducens nucleus, of the trigeminus and oculomotorius nuclei are in a similar condition.

The cells of Purkinje in the cerebellum are intensely altered, enlarged, and with the exception of the nucleus are structureless, so that they are found with difficulty.

FIG. 1.



Cells of the anterior horn in the lumbar region in a case presenting the symptoms of meningitis. The pathological changes consist of an alteration of the nerve cells like that of amaurotic family idiocy. The cells are represented as they appear in one field of the microscope, in order to show the intense alteration of all the cells.

The nerve cells of the paracentral lobule, the small cells as well as the cells of Betz, and those of the frontal and occipital lobes are in a similar condition.

I have not been able to find a single normal nerve cell in the central nervous system.

The Marchi method shows most intense alteration of the white matter in the brain and cord, especially in the former.

The crossed pyramidal tracts do not contain black dots in the lumbar region, as the degeneration here is of long standing. The nerve fibres of the anterior horns show some degeneration by the Marchi method.

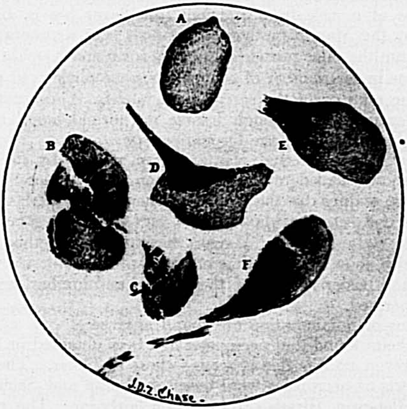
The crossed pyramidal tracts in the midthoracic region show a little recent degeneration, as do also the direct cerebellar tracts.

The same condition is found in the lower cervical region. The posterior columns are not degenerated.

The nerve fibres within the lower olives are much degenerated.

In the pons the intramedullary portion of the trigeminus, the lemniscus, the fibres crossing in the raphe, the superior cerebellar peduncle are much degenerated. The degeneration of the motor tracts is of longer duration than is that of many of the other tracts of the pons, but is still very intense, and much more so than is the degeneration of the pyramidal tracts in the cord as shown by the Marchi method. Indeed, an examination of the sections leads one to conclude that the motor tracts may have degenerated earlier in the cord than in the brain.

FIG. 2.



Cells from the same case as represented in Fig. 1, selected from the anterior horns of the lumbar region, with the exception of cell *E*, which is from the paracentral lobule. Cell *A* shows complete chromatolysis. Cells *B* and *C* are broken into several fragments. In cells *D*, *E*, and *F* the chromophilic elements are seen only in one part of the cell body, and the nucleus is not distinct. By comparing Figs. 1 and 2 with the illustrations in the paper by Hirsch and Sachs it will be seen that the alterations are exactly like those of amaurotic family idiocy.

The foot of the cerebral peduncle is much degenerated, but the degeneration is of long duration, and is more intense in the dorsal portion of the foot, and here the fatty granular cells are very numerous, especially about the bloodvessels. There is comparatively little free degenerated myelin in the foot of the peduncle, and the numerous fatty granular cells stain deeply by the Marchi method.

This seems to indicate that the degeneration had existed long enough for the myelin to be absorbed by these cells.

Intramedullary fibres of the oculomotor nerve show a moderate amount of recent degeneration by the Marchi method.

The superior cerebellar peduncle is much degenerated and contains much free myelin.

The posterior longitudinal bundle may be slightly degenerated.

The lemniscus is considerably degenerated.

The white matter of the occipital and frontal lobes and of the paracentral lobule is much degenerated by the Marchi method.

Sections taken from the middle of the upper part of the corpus callosum are intensely degenerated by the Marchi method.

A piece of muscle from the foot, the flexor brevis digitorum, stained by the Marchi method shows no recent degeneration, but a piece from the same muscle stained by eosin and hæmalum shows an increase in the number of connective-tissue nuclei and probably also in the number of the sarcolemma nuclei. The muscle fibres appear degenerated, although I have no normal muscles from a child of about the same age for comparison.

A piece of one internal plantar nerve stained by the Marchi method shows considerable degeneration, but a piece from the same nerve stained by the Weigert hæmatoxylin method or acid fuchsin is not degenerated or at least very slightly degenerated.

Sections stained by the Weigert hæmatoxylin method or acid fuchsin also show degeneration of the central motor tracts. The anterior and posterior roots of the cervical and lumbar regions are not degenerated.

No signs of inflammation are found anywhere.

Falkenheim found that necropsies had been obtained in 11 cases; in 2, however, no report was made—those of Grosz. The 9 cases with reports of necropsies were those of Knapp and Sachs, Kingdon (3), Peterson, Hirsch, Mohr, and Clairborne. The report of necropsy in Clairborne's case is exceedingly brief. Since Falkenheim's paper appeared cases with necropsy have been reported by Frey (1), Schaffer (1), and Sachs (1). In Mohr's case the report of the histological examination was written by Schaffer.

Falkenheim says that in amaurotic family idiocy the degeneration of the pyramidal tracts has been followed through the cerebral peduncles, pons, medulla oblongata, and spinal cord. The lemniscus also has been found degenerated, as well as the tangential fibres, the spinal root of the fifth nerve, the anterior cerebellar peduncle, the columns of Goll, and the optic nerves. Falkenheim mentions Hirsch's paper, but he does not do justice to the latter's cellular findings.

Schaffer[1] found intense and widely diffused degeneration of the brain and degeneration of the pyramidal tracts of the spinal cord. The gray matter of the cord was not diseased. No mention is made of the condition of the nerve cells of the brain. This is not the same case as the one described in Mohr's paper.

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[1] Wiener klin. Rundschau, 1902, p. 324.

Frey's case is especially interesting because his is one of the very few in which the Marchi method has been employed in the study of a case of amaurotic family idiocy. He found increased consistency of the brain and spinal cord. The crossed pyramidal tracts, the tracts of Gowers, and the lateral border zones (Grenzschichten) were degenerated. The direct cerebellar tracts and the anterior columns were normal. The degeneration of the posterior columns, especially of the columns of Goll, began in the lower thoracic region and could be followed to the nuclei of the columns of Goll. The fibre reticulum of the anterior horns had almost disappeared in the cervical region. The white matter of the brain showed much degeneration. It is probable that the peculiar cellular alterations of amaurotic family idiocy were present in this case, although Nissl's method could not be employed. Frey[1] says that the pyramidal cells of the cortex were rounded and had lost their normal shape. There was no trace of inflammation. Evidently the peculiar cellular alteration of this disease escaped him, as he does not speak explicitly about it, and does not appear to have read Hirsch's paper. The optic tract and chiasm were degenerated but the optic nerves were normal. The entire central nervous system was affected.

He refers to another case of the disease that he was studying in which a pronounced degeneration of the nerve cells with vacuolation was found, but there seems to have been little to him that was characteristic in this cellular alteration.

Sachs'[2] recent paper fully confirms the extraordinary cellular findings described by Hirsch in a case of amaurotic family idiocy, and these seem to be the only cases in which this peculiar and widespread cellular degeneration was reported, except that Sachs now believes that some of his earlier cases showed a similar alteration.

The description of the changes of the nerve cells in my report conforms very closely with those given by Hirsch[3] and Sachs.

If the widespread and intense cellular alteration is a common condition in amaurotic family idiocy it is remarkable that, according to Falkenheim, the electric irritability of the muscle is preserved, and that only Koplik and Grosz have found slowing or diminution of the faradic contractility.

Russell and Kingdon[4] stated in 1899 that no changes in the peripheral nerves had been found in amaurotic family idiocy, and

[1] Neurologisches Centralblatt, September 16, 1901, p. 836.

[2] Journal of Nervous and Mental Disease, 1903, p. 1.

[3] Ibid., 1898, p. 538.

[4] Allbutt's System of Medicine, The Macmillan Co., 1899, vol. viii. p. 728.

I have not been able to find the report of any such changes recorded in the literature.

In the case that I have studied the piece removed from the internal plantar nerve was distinctly degenerated by the Marchi method.

I do not share Sachs' opinion that the changes in the nerve cells in the cases of Rolly, Collier, and Mya and Levi were like those of amaurotic family idiocy. Rolly[1] says that in the lumbar region the processes of the ganglion cells were abnormally intensely stained, and the portion of the processes that normally does not stain took the stain. The nerve cells were least altered in the lumbar region. Near ganglion cells that were entirely normal were others in which chromatolysis had occurred, in some this was perinuclear while the chromophilic elements at the periphery of the cell were preserved. Some cells showed peripheral chromatolysis while the chromophilic elements about the nucleus were preserved. Nowhere was there any marked alteration of the form of the cell.

The changes in the nerve cells of the thoracic region were like those of the lumbar region.

The changes in the cervical region were more intense. Normal cells were less numerous than elsewhere in the spinal cord, and chromatolysis was more pronounced. Still more intense were the changes in the brain. Nowhere does Rolly speak of a swelling of the cell, with destruction of the cell processes, and complete loss of all stainable portions of the cell except about the nucleus, which is displaced to the periphery. Nor was the alteration by any means found in all the nerve cells. The alteration of the nerve cells was pronounced in Rolly's case, but, as a study of his drawings show, it was very unlike that of amaurotic family idiocy. The pyramidal tracts were perfectly normal.

In two cases, one of cerebral diplegia and one of generalized rigidity, with necropsy reported by J. S. Collier,[2] the cellular alteration was not like that of amaurotic family idiocy. The pathological report in these two cases is by Risien Russell. In the first case there was a great paucity of nerve cells in the cerebral cortex. Neither the cells nor their nuclei presented any signs of swelling. Many of the cells preserved more or less their normal pyramidal shape, but they were all below the normal in size, many of them very much so. The cells stained diffusely by the Nissl method. The pyramidal tracts were degenerated.

In the second case the cellular alteration and the degeneration of the pyramidal tracts were very similar. The changes in the nerve cells in these cases were not at all like those of amaurotic family idiocy.

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[1] Deutsche Zeitschrift f. Nervenheilkunde, Bd. xx. p. 152.

[2] Brain, 1899, vol. xxii. p. 378.

So far as I can determine the changes in the nerve cells described by Mya and Levi were not those of amaurotic family idiocy.

In 1899, in association with Dr. D. J. McCarthy,[1] I reported a case not of amaurotic family idiocy, with changes in the nerve cells, however, like those occurring in this disease. The patient, a girl, was nine years old at the time of her death. Her sight was said to be good, but it is not known that any visual examination was made. She could not speak. She had a normal gait earlier in life. She began to walk before she was two years of age and had no motor paralysis. She never had convulsions. The feet and hands were always cold. She was said to be lacking in sensation, and would handle hot coals or hot food without making a sound of discomfort. She was exceedingly active and noisy, wet her bed and day clothing, did not understand what was said to her, and could not read. During the year previous to her death she showed gradual emaciation, but no cause could be detected for this. The gait was observed to be more shambling than previously. Emaciation became extreme before death.

At the necropsy the bridge of the nose was found flattened, the lower front teeth were nicked like those known as Hutchinson's teeth, the sternum was prominent. Internal hemorrhagic pachymeningitis was found on each side of the brain. The pia was very œdematous and the brain was quite soft. The nerve cells of the paracentral lobule, of the frontal lobe and posterior portion of the parietal lobe, of the cerebellum and bulbar nuclei, and of the anterior horns of the cervical and lumbar regions were swollen and altered in the manner described more in detail in the following case. The capillaries in the cerebral cortex and in the spinal cord were very numerous and congested. Secondary degeneration in the spinal cord was not present, even by the Marchi method.

These remarkable cellular changes throughout the central nervous system were described in detail and were represented by drawings. Reference also was made in that paper to the similar condition described by Hirsch in amaurotic family idiocy. Microscopic examination showed that in our case the optic nerves were normal. It was thought that the œdema of the cortex possibly might explain the alteration of the nerve cells, although it was acknowledged that the cases of uræmia reported in literature did not justify this view.

In 1900 I observed again changes in the nerve cells that were exactly like those occurring in amaurotic family idiocy in another case that could not be considered as typical of this disease. The patient, a boy, was within three months of eight years of age at the time of his death. The notes were incomplete, but it is recorded that he was of feeble mental development, did not know the alphabet, did not talk, and could not dress himself properly. His sight and hearing were said to be good, although it is doubtful whether there was a visual examination. His gait was spastic. He was small and had scoliosis. Sensation was normal so far as could be determined. He did not have convulsions. He died with symptoms of cerebrospinal meningitis.

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[1] Journal of Nervous and Mental Disease, November, 1899, p. 677. Spiller, ibid., 1901, p. 140.

At the necropsy a large amount of cerebrospinal fluid escaped when the calvarium was removed. The brain was œdematous. The microscopic examination of the nervous tissues showed little evidence of inflammation. The nerve cells throughout the central nervous system were greatly altered, those in the posterior as well as those in the anterior horns of the spinal cord, the cells of the nuclei of the cranial nerves, sensory as well as motor, the cells of Purkinje and those in the parietal lobe, especially the cells of Betz, were all affected. The cell-body everywhere was swollen and rounded, many of the dendritic processes had disappeared; the chromophilic elements were seen only in one portion of the cell, and here they surrounded the nucleus, and even here they were more or less disintegrated, and the nucleus was at the periphery of the cell-body. Numerous small bacilli were found within the nervous tissues, but these may have entered the tissues after death.

In neither of these two extraordinary cases was secondary degeneration found, even by the Marchi method. Both children were of very feeble mentality, and were from the Pennsylvania Training School for Feeble-minded Children. It is incomprehensible that any function could be possible with such intense and general alteration of the nerve cells, and it is improbable that such an alteration could have existed a long time.

No one has been able to make a thorough microscopic study of the early degeneration of amaurotic family idiocy, and in those cases in which a microscopic examination has been made the disease had reached its full development and had been the cause of death. What the primary alterations are in this disease we do not know, but the widespread cellular alteration and comparatively slight changes in the white matter in the two cases referred to by me suggest that the cells probably are first diseased in amaurotic family idiocy, but this is by no means certain.

I cannot, any more than does Sachs, accept the view that amaurotic family idiocy is a toxic or acquired disease. Sachs, in referring to my second paper, remarks that I seem to interpret the cell changes as the result of the acute process in the cases to which I have referred above. The sentence to which he refers probably is this: "A theory of a toxic condition in the second case could be well supported by the clinical history, but not so well in the case of internal hemorrhagic pachymeningitis, although even in this it could not be absolutely rejected." I think I imply a very decided doubt regarding the nature of the process. Indeed, I feel unable to say why in the two cases to which I have referred such an extraordinary pathological condition was found. These two cases are unique in the literature so far as I know, and, therefore, their interpretation at present should be left in doubt. They show a remarkable resemblance in their pathological findings to those of amaurotic family idiocy, and I am tempted to suggest that *possibly* they were aberrant types of this disease. In neither case was the clinical history complete and in neither case was an examination of the eye-grounds made.

It is important in this connection to mention that the first child to whom I have referred, who was the third child in the family, had a sister three years her senior, the second child in the family, who also died in a home for feeble-minded children, at the age of eight years, from what was supposed to be "tuberculous meningitis." It is very doubtful whether a microscopic examination or even a careful gross examination was made in this case. The two sisters were said to be so alike that the parents had only one photograph taken as representing both children. In my second case death occurred following symptoms suggestive of meningitis, and a number of children with amaurotic family idiocy have died with symptoms of meningitis.

Can there be a type of disease resembling closely amaurotic family idiocy but causing death about the eighth or ninth year of life, instead of within the second year of life? It seems to me that this is possible, because the alteration of the cells throughout the nervous system, in the two cases I have referred to, is entirely unlike anything occurring in other forms of imbecility and spasticity, and is so striking that anyone who has seen it once can never mistake it.

Russell and Kingdon say that two cases of amaurotic family idiocy have been reported in which death did not occur in the earliest years (they are those of Koller[1] and Peterson[2]), but Falkenheim remarks that these two cases were the same, so that really there was only one with a delayed fatal termination. The case is not with necropsy. Peterson mentions that in this case blindness was noticed when the child was six months old. At the time Peterson wrote his paper the child was five and a half years old and was an idiot. Falkenheim says that in 64 cases of amaurotic idiocy reported, death is mentioned as occurring in 38. Two patients died in the first half of the third year of life, one when three and a half years old, and the others before the end of the second year.

It is doubtful whether the case reported by Hirschberg[3] should be regarded as one of amaurotic family idiocy. His patient was fifteen years of age.

Falkenheim mentions that the characteristic ocular changes were not found in all cases of amaurotic family idiocy, so that the uncertainty concerning the existence of ocular changes in my two cases is of less importance. The absence of ocular changes must make the diagnosis difficult.

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[1] New York Medical Record, 1896, p. 266.

[2] Journal of Nervous and Mental Disease, 1898, p. 529.

[3] Centralblatt für Augenheilkunde, January, 1904.

A CASE OF CARCINOMA OF THE URETER APPARENTLY INDUCED BY A CALCULUS LODGED IN ITS JUXTAVESICAL PORTION.[1]

By William F. Metcalf, M.D.,
and
Homer E. Safford, M.D.,
of Detroit.

I. Clinical. The following case is presented largely for its pathological interest, some of its features being so extraordinary as to make some report of it scientifically imperative. The surgical treatment will be given in some detail, although, in the light of subsequent developments in the case, a different course would be pursued were a similar one again confronted. The safety of the measures adopted for relief is confirmed by the satisfactory recovery from the operation itself, while the failure ultimately to save the patient's life depended upon circumstances beyond my control.

The patient, Mr. J. H., aged forty-seven years, was admitted to Harper Hospital on October 29, 1903. His father had died, at seventy-six years, of Bright's disease; his mother was living. The maternal grandfather died of tuberculosis, as did also two maternal uncles. One maternal uncle died of epithelioma upon the face. One sister died in infancy; two brothers died of typhoid fever.

From the fourth to the twenty-fifth year of the patient's life he suffered frequent attacks of what he called "bellyache," more severe in the left side of the abdomen and radiating toward the testicle. It was said to be followed by a feeling of coldness in the centre of the abdomen. During his twenty-fifth year, he had a severe attack lasting from June until August, when the appearance of sudden relief was attended with a profuse discharge by the urethra. He was then free from pain for three years, at the end of which time occurred another severe attack of pain, lasting two days, and likewise followed by sudden relief. Two or three such attacks followed during the next ten years, and during the same interval he had occasional chills and fever.

September 1, 1903, he began to have severe cramping pain in

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[1] Read before the Michigan State Medical Society (Surgical Section), Grand Rapids, May 26, 1904.